Kidney International, Vol. 52 (1997), pp. 1084–1088

Pressure or flow recordings for the surveillance of hemodialysis grafts

PETER J. BOSMAN, FRANS T.J. BOEREBOOM, HENK F.M. SMITS, BERT C. EIKELBOOM, HEIN A. KOOMANS, and PETER J. BLANKESTIJN

Departments of Nephrology, Radiology, and Vascular Surgery, University Hospital Utrecht, Utrecht, The Netherlands

Pressure or flow recordings for the surveillance of hemodialysis grafts. Venous pressures (VP) measured by the dialysis machine are widely used for access surveillance and have significantly improved outcomes. VP reflect the resistance in the venous outflow tract, which will rise in the presence of stenosis. Low graft flow caused by high graft resistance predicts thrombosis. In this study we investigated whether high VP coincides with low graft flow (measured by ultrasound dilution technique). Of 70 forearm bridge grafts in 42 chronic hemodialysis patients, 31 had an angiographically proven outflow stenosis. VP at 200 ml/min blood flow (VP200), total graft resistance and venous outflow resistance were higher whereas graft flow was lower in patients with venous outflow tract stenosis as compared to patients without stenosis. Diagnostic power of the tests for identifying patients with venous stenosis showed no important differences. However, arterial inflow resistance, which is not reflected in VP measurements, represented a substantial and, more importantly, a highly variable percentage of total graft resistance. As a result graft flow showed no correlation with VP measurements. In conclusion, although patients with venous outflow stenosis may be identified accurately using venous pressure assessments, graft flow measurements seem to be more suitable for selecting patients at risk for thrombosis.

Vascular access thrombosis is an important problem in the management of patients on chronic hemodialysis, and to identify patients at risk is a challenge for the clinician [1]. In the majority of cases, thrombosis is associated with the presence of one or more stenoses, usually located in the venous outflow tract [2–5]. Thus, the present strategy of graft surveillance is focused on diagnosing venous outflow tract stenosis [6–10], for which purpose angiography is very sensitive and is accepted as the "gold standard." Because angiography is not very practical, the more usual surveillance strategy is measurement of venous drip chamber pressures (VP) [11] or intragraft pressures [12]. Both will rise if venous outflow resistance increases.

Based on rheological data, one can surmise that a high local resistance together with a low blood flow is the ideal combination to provoke thrombosis. Conceivably, venous outflow tract stenosis causes both, making an association between venous outflow tract stenosis, low graft flow and thrombosis likely. However, the actual determinants of graft flow are blood pressure, which is variable, and total graft resistance, which is determined to a substantial degree by arterial inflow resistance [13]. VP measurements do not inform on these variables. Thus, elevated VP measurements may be a useful indicator of venous outflow tract stenosis, but it is unclear if they coincide low graft blood flow. If they do, it does not seem necessary to use more troublesome surveillance methods than VP, but if they do not, VP may not be as predictive for thrombosis as graft blood flow. However, we are not aware of any formal study of the relationship between VP or outflow resistance and spontaneous graft flow. Recent technical developments have made it possible to reliably assess graft blood flow [14, 15], and thus to estimate total graft resistance, as well as inflow and outflow resistances. Therefore, our aim was to compare spontaneous graft blood flow and calculated graft resistance on the one hand, and VP or outflow resistance on the other hand in a group of dialysis patients with and without venous outflow tract stenosis.

METHODS

Patients

We evaluated the data of 70 grafts in 42 (11 male) chronic hemodialysis patients. Patients who were evaluated more than once, had either a different graft or had undergone an angioplasty or surgical intervention on the second or later occasion. All patients had an arteriovenous bridge graft (21 polytetrafluoroethelene, PTFE, in 15 patients and 49 denatured homologous veins in 27 patients) in the forearm, that is, a looped graft between the brachial artery and cephalic vein, or, in two cases, a straight graft from the radial artery to the cephalic vein. Patients were asked to participate regardless of the clinical performance of the graft. All pressure and flow measurements were done in the first 30 minutes of a single and same dialysis session.

Pressure measurements

Pressure measurements were performed by a Gambro AK100 dialysis machine using a standard Gambro tubing set and two 15Gx25 mm Gambro needles. With this device venous drip chamber pressure (VP) and pressure in the arterial line (AP) of the circuit can be monitored continuously on a digital display. All measurements were done in a standardized way with the access on the level of the venous drip chamber.

VP was assessed at a dialysis machine blood flow of 200 (VP200) and of 0 ml/min (VP0) with open graft. Subsequently, the graft was compressed between the venous and arterial needles,

Received for publication March 17, 1997
and in revised form May 30, 1997
Accepted for publication June 2, 1997

Table 1. Results of pressure and flow measurements and calculation of resistances in patients without (Group A, N = 39) and with (Group B, N = 31) an angiographically documented stenosis in the venous outflow tract

	No graft stenosis (group A)		Graft stenosis (group B)		
	Mean	SD	Mean	SD	Significance
VP200 *mm Hg*	95	22	126	35	< 0.001
VP0 *mm Hg*	26	21	49	27	< 0.001
Flow *ml/min*	1061	541	664	389	= 0.002
Relative outflow resistance	0.315	0.165	0.537	0.187	< 0.001
Mean blood pressure *mm Hg*	95	20	88	21	NS
Graft resistance *U*	0.153	0.214	0.192	0.133	= 0.011
Inflow resistance *U*	0.111	0.160	0.088	0.074	NS
Outflow resistance *U*	0.043	0.066	0.104	0.095	< 0.001

Significance indicates the P values of the differences between Groups A and B.

and, after 10 seconds of stabilization, pressures in the venous line and arterial line were measured with dialyzer blood flow turned off (VPcomp0 and APcomp0). The results contained the averages of 10 subsequent readings on the display.

Flow measurements

Flow was measured with the Transonic Hemodialysis Monitor (Transonic Systems Inc., Ithaca, NY, USA). The theoretical background, bench validation and *in vivo* validation are described in detail in previous papers [14, 15]. In short, the patients had two needles in the graft, one facing the arterial anastomosis and the other facing the venous anastomosis. To measure graft flow the dialyzer lines were reversed from normal: the arterial inlet was downstream to the venous outlet, and the outlet now faced the graft stream. Flow sensors were clipped on the arterial and venous blood lines to measure dialyzer blood flow and to record ultrasound dilution caused by saline bolus injections (5 ml). These indicator injections were administered in the venous blood line upstream from the venous sensor. The indicator was mixed with the blood flowing in the graft. The fraction of the indicator detected by the sensor on the arterial line was determined by the ratio between flows in the extracorporeal circuit (which was known) and the graft. Flow determinations consisted of five single measurements, which were averaged. All measurements were done during a fixed dialyzer blood flow, usually 200 ml/min. Ultrafiltration was turned off three minutes before the start of the measurements to avoid the effect of hemoconcentration during the measurements.

Angiography

An angiogram was made in all patients. The time interval between the pressure and flow measurements and the angiogram was usually less than two weeks and never longer than four weeks, and venous pressures were stable throughout that time. In most cases, the angiogram was made immediately before a dialysis session by injecting the contrast medium through the venous dialysis needle. The objective was to visualize the graft and the venous outflow tract up to the subclavian vein. We used a standardized protocol for angiograms, which included at least two projections of the venous outflow tract. A reduction of luminal diameter of more than 50% as compared to the adjacent vein was considered significant. All angiograms were reviewed by a radiologist who was unaware of VP and flow measurements.

Calculations and statistical analysis

VP0 is the spontaneous pressure in the graft at the venous needle insertion site. The pressure drop over the whole graft flow tract, that is, from the left ventricle to the right atrium was calculated by (APcomp0 − VP comp0), where VPcomp0 is the central VP and APcomp0 represents the arterial pressure. Total graft resistance was calculated from [(APcomp0 − VP comp0)/graft flow]. Arterial inflow and venous outflow graft resistances were calculated from, respectively, [(APcomp0 − VP0)/graft flow] and [(VP0 − VPcomp0)/graft flow]. We cannot exclude a slight overestimation of resistances due to rise of AP and fall of VP during compression of the graft. Relative venous outflow resistance was estimated as the ratio of venous outflow and total graft resistances [13].

VP200, being the venous drip chamber pressure at a dialyzer flow of 200 ml/min, represents the usual but indirect clinical indicator of graft venous outflow resistance.

The Mann-Whitney U-test was used to compare the distribution of a variable between two nonrelated groups (SPSS for Windows). To determine the best discriminating parameter for the existence of venous outflow tract stenosis, receiver operating characteristics (ROC) curves were made, and areas under the curves (AUC) were calculated [16]. Differences between the AUCS were tested with the method of Hanley and McNeil [17]. A P value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Patients were divided according to absence or presence of a significant stenosis in the venous outflow tract as established by angiography. In 39 cases no stenosis was found (group A). In the other 31 cases (group B) one or more significant stenoses were found, either at the venous anastomosis or in the adjacent veins (N = 29 in 21 patients) or in the subclavian vein (N = 2 in 2 patients).

The average values of VP200, total graft resistance, venous outflow resistance, and relative venous outflow resistance were each significantly higher in group B than in group A, whereas graft blood flow was significantly lower in group B (Table 1). However, as illustrated in Figure 1, there was some overlap of the individual data for each of these indicators. In the ROC curve analysis the values (AUC ± SEM) for these indicators were 0.852 ± 0.048 for outflow resistance, 0.833 ± 0.046 for VP200, 0.813 ± 0.053 for

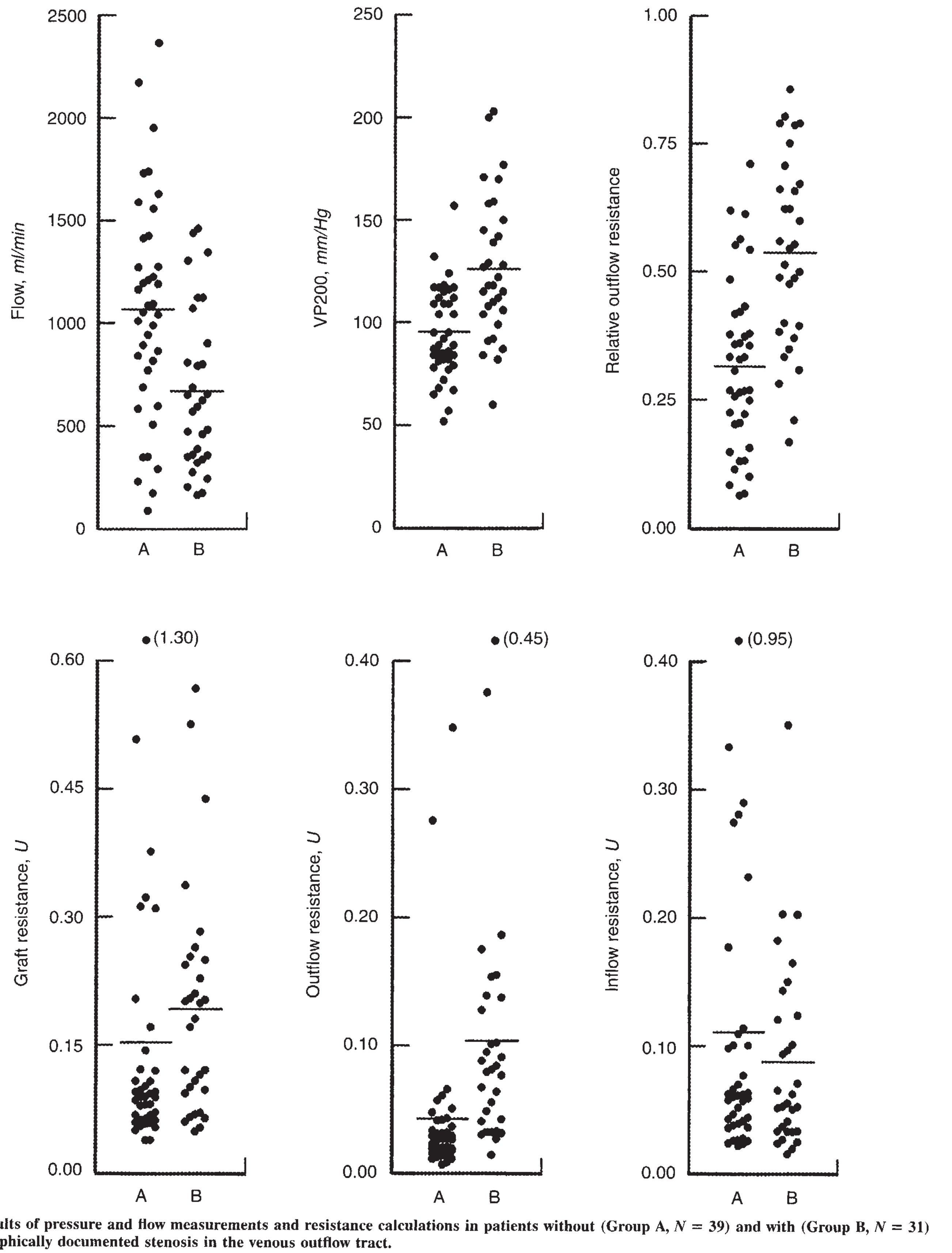

Fig. 1. Results of pressure and flow measurements and resistance calculations in patients without (Group A, $N = 39$) and with (Group B, $N = 31$) an angiographically documented stenosis in the venous outflow tract.

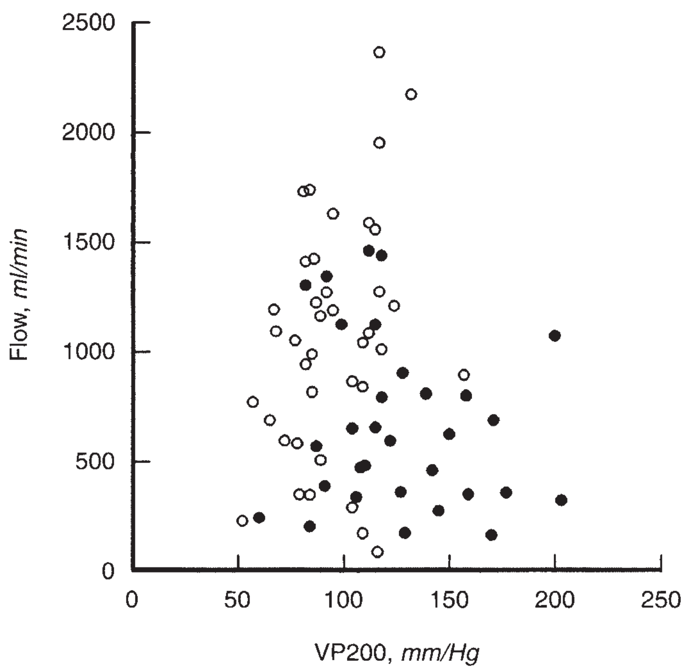

Fig. 2. Relation between VP200 and graft flow. Symbols are: (●) patients with stenosis in the venous outflow tract; (○) patients without stenosis in the venous outflow tract.

relative outflow resistance, 0.752 ± 0.063 for VP0, 0.716 ± 0.063 for graft flow, and 0.679 ± 0.065 for total graft resistance. The AUC of outflow resistance was significantly different from that of graft flow and of total graft resistance. Other differences were not significant. Thus, the discriminating power of the different tests for detecting stenosis in the venous outflow tract were not better than the regularly used indicator (VP200). Results of pressure and flow measurements and calculated resistances of PTFE and denatured homologous vein grafts showed no significant differences.

Average arterial pressures did not differ between the two groups (Table 1). The average arterial inflow resistances were also similar, implicating that the differences in total graft resistance between groups A and B were due to differences in the venous outflow resistance. However, both arterial pressure and inflow resistance showed large interindividual differences in each group (Fig. 1), which could disturb the relation between graft flow and (indicators of) venous outflow resistance. Indeed, VP200 correlated well with relative and absolute outflow resistance ($r = 0.728$, $P < 0.001$ and $r = 0.445$, $P < 0.001$, respectively), whereas no correlation was found between VP200 and graft flow ($r = -0.127$, P = NS) and between VP200 and total graft resistance ($r = 0.108$, P = NS). Figure 2 gives a plot for flow and VP200.

DISCUSSION

The present study in patients with forearm grafts shows that VP measurements correlate strongly with outflow resistance. The data also show that segmental inflow resistance determines a substantial and highly variable portion of the total graft resistance. As a consequence, VP measurements do not correlate with graft flow or total resistance.

In hemodialysis patients with an arteriovenous graft, stenoses tend to develop for yet unknown reasons, typically in the venous outflow tract [2–5]. The present policy of graft surveillance is directed towards detecting these stenoses [6–10], for which purpose a high VP at fixed blood flow [11] or zero dialyzer blood flow [12] is commonly used. However, the risk for graft thrombosis may not be determined by the degree of luminal reduction *per se*, but by its combined occurrence with a low graft flow. Indeed, several studies have indicated that low flow indicates imminent thrombosis [18–23]. In this cross sectional study of random dialysis patients, the VP200 method does not predict graft blood flow (Fig. 2). Our data indicate that the resistance along bridge grafts without outflow tract stenosis was distributed over the arterial and venous sides in an average ratio of 3:1, similar as found by others [13, 24]. This implies that an increase of venous resistance by 100% will increase total graft resistance by only 25%, and thus has only modest impact or graft flow. Moreover, the overall variation in inflow resistance, from 0.016 to 0.948 U (Fig. 1) in the whole group, is so large that this factor is a major determinant of graft blood flow. In fact, the impact of inflow resistance variation is larger than the impact imposed by the average threefold difference in venous outflow tract resistance found between patients with and without venous outflow tract stenosis. This is illustrated by the occasional observation of a high graft blood flow in individuals with documented venous outflow tract stenosis, or an extremely low blood flow in patients without venous outflow tract stenosis (Fig. 2).

The data are of clinical relevance because they indicate that with measurements of VP200, VP0 or relative outflow resistance, the latter being basically identical to the ratio of intragraft pressure and arterial pressure [12], we may accurately select patients with outflow tract stenosis, but we will be unable to identify all patients with increased risk for thrombosis. Patients with an arterial inflow or midgraft stenosis and patients with overall poor quality of the graft will be missed with VP measurements. These data may offer an explanation why, in a patient population in which VP measurements were used to select patients for corrective interventions, the thrombosis rate may decrease but will certainly not be abolished [11, 12].

This cross sectional study does not tell us about the level of flow or resistance at which the risk for thrombosis increases. A limited number of studies using different techniques [18–21, 23] and one study using the present technique [22] have addressed this question. The available data suggest that grafts showing a flow below approximately 600 ml/min are at risk for thrombosis. Based on the above-mentioned considerations, we suggest that graft surveillance should include regular flow measurements. By calculating resistance, changes in flow caused by differences in blood pressure can be differentiated from those due to changes in the anatomy, for instance, those that are caused by developing stenosis. In the patients with low flow and high resistance a subsequent angiogram should define the correctable anatomical lesions. It is important to realize that some data suggest that the interruption of the thrombosis, such as declotting or rethrombosis cycle by elective angioplasty, may indeed increase the longevity of grafts [12].

In conclusion, our data show that measurement of dialyzer venous drip chamber pressure at fixed dialyzer blood flow is quite adequate for the detection of a stenosis in the venous outflow tract. However, it is also clear that venous outflow resistance is only one of the determinants of graft flow, which shows wide variation irrespective the quality of the venous outflow tract.

Assuming that the combination of low graft flow and high graft resistance constitutes a risk for thrombosis, our data imply that both should be monitored longitudinally in individuals. Prospective studies are needed to test this hypothesis.

ACKNOWLEDGMENTS

Peter J. Bosman is supported by the Dutch Kidney Foundation, grant C94.1356. We thank Dr. Yvonne T. van der Schouw for her assistance with the statistical analysis.

Reprint requests to Peter J. Blankestijn, M.D., Department of Nephrology and Hypertension, University Hospital Utrecht, Room F03.226, PO Box 85500, 3508 GA Utrecht, The Netherlands.

REFERENCES

1. Blankestijn PJ, Bosman PJ, Boereboom FTJ: Hemodialysis access without thrombosis: Is it possible? (Editorial Comment) *Nephrol Dial Transplant* 12:2394–2397, 1996
2. Valji K, Bookstein JJ, Roberts AC, Davis GB: Pharmacomechanical thrombolysis and angioplasty in the management of clotted hemodialysis grafts: Early and late clinical results. *Radiology* 178:243–247, 1991
3. Beathard GA: Mechanical versus pharmacomechanical thrombolysis for the treatment of thrombosed dialysis access grafts. *Kidney Int* 45:1401–1406, 1994
4. Kanterman RY, Vesely TM, Pilgram TK, Guy BW, Windus DW, Picus D: Dialysis access grafts: Anatomic location of venous stenosis and results of angioplasty. *Radiology* 195:135–139, 1995
5. Smits HFM, van Rijk PP, van Isselt JW, Mali WPTM, Koomans HA, Blankestijn PJ: Pulmonary embolism after thrombolysis of hemodialysis grafts. *J Am Soc Nephrol* (in press)
6. Fan PY, Schwab SJ: Vascular access: Concept for the 1990s. (Editorial Review) *J Am Soc Nephrol* 3:1–11, 1992
7. Windus DW: Parmanent vascular access: A nephrologist's view. *Am J Kid Dis* 21:457–471, 1993
8. Porile JL, Richter M: Preservation of vascular access. *J Am Soc Nephrol* 4:997–1003, 1993
9. Depner TA: Techniques for prospective detection of venous stenosis. *Adv Renal Replac Ther* 1:119–130, 1994
10. Besarab A, Frinak S, Zasuwa G: Prospective evaluation of vascular access function: The nephrologist's perspective. *Semin Dial* 9(Suppl 1):S21–S29, 1996
11. Schwab SJ, Raymond JR, Saeed M, Newman GE, Dennis PA, Randal Bollinger R: Prevention of hemodialysis fistula thrombosis. Early detection of venous stenosis. *Kidney Int* 36:707–711, 1989
12. Besarab AS, Sullivan KL, Ross RP, Moritz MJ: Utility of intragraft pressure monitoring in detecting and correcting outlet stenoses prior to surgery. *Kidney Int* 47:1364–1373, 1995
13. Van Stone JC, Jones MJ, van Stone J: Detection of hemodialysis access outlet stenosis by measuring outlet resistance. *Am J Kid Dis* 23:562–568, 1994
14. Krivitski NM: Theory and validation of access flow measurement by dilution technique during hemodialysis. *Kidney Int* 48:244–250, 1995
15. Bosman PJ, Boereboom FTJ, Bakker CJ, Mali WPT, Eikelboom BC, Blankestijn PJ, Koomans HA: Access flow measurements in hemodialysis patients: In vivo validation of an ultrasound dilution technique. *J Am Soc Nephrol* 7:966–969, 1996
16. Hanley JA, McNeil BJ: The meaning and use of the area under receiver operating characteristics (ROC) curves. *Radiology* 143:29–36, 1983
17. Hanley JA, McNeil BJ: A method of comparing the areas under receiver operating characteristics curves derived from the same cases. *Radiology* 148:839–843, 1983
18. Rittgers SE, Garcia-Valdez C, McCormick JT, Posner MP: Noninvasive blood flow measurement in expanded polytetrafluoroethylene grafts for hemodialysis access. *J Vasc Surg* 13:635–642, 1986
19. Shackleton CR, Taylor DC, Buckley AR, Rowley A, Cooperberg PL, Fry PD: Predicting failure in polytetrafluoroethylene vascular access grafts for hemodialysis: A pilot study. *Can J Surg* 30:442–444, 1987
20. Strauch BS, O'Connell RS, Geoly KL, Grundlehner M, Yakub N, Tietjen DP: Forecasting thrombosis of vascular access with Doppler color flow imaging. *Am J Kid Dis* 19:554–557, 1992
21. Köksoy C, Kuzu A, Erden I, Türkçapar AG, Düzgun I, Anadol E: Predictive value of colour Doppler ultrasonography in detecting failure of vascular access grafts. *Br J Surg* 82:50–52, 1995
22. Depner TA, Reasons AM: Longevity of peripheral A-V grafts and fistulas for hemodialysis is related to access blood flow. (abstract) *J Am Soc Nephrol* 7:1405, 1996
23. Lindsay RM, Blake PG, Malek P, Posen G, Martin B, Bradfield E: The measurement hemodialysis access blood flow rates by the hemodynamic monitor. (abstract) *J Am Soc Nephrol* 7:1412, 1996
24. Sullivan KL, Besarab A, Bonn J, Shapiro MJ, Gardiner GA, Moritz MJ: Hemodynamics of failing dialysis grafts. *Radiology* 186: 867–872, 1993